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Reduced prognostic value of elevated Beta-2-microglobulin levels on time to first treatment in newly diagnosed CLL patients with compromised kidney function

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Introduction:

The clinical course of newly diagnosed CLL is extremely heterogeneous. Predictive indices, such as the CLL-IPI were developed to help identify patients who require therapy relatively soon after diagnosis. Besides dysfunctional TP53 and unmutated IGHV status, elevated beta-2-microglobulin (B2M) plasma levels were shown to most effectively identify patients at high risk for short time to first therapy (TTFT) in the weighted risk score of the CLL-IPI.
However, B2M plasma levels are commonly elevated in patients with chronic kidney disease (CKD) and the CLL-IPI has not been adjusted for compromised kidney function.

Methods:

Between 2000 and 2022, newly diagnosed CLL patients not fulfilling criteria for immediate specific treatment were identified from the clinical database at a tertiary care center in Innsbruck, Austria. TTFT was stratified according to the CLL-IPI and CKD (GFR < 60 ml/min). B2M plasma levels were compared in CKD and non-CKD patients. In CKD patients with elevated B2M plasma levels (> 3.5 mg/L), the CLL-IPI was reviewed to check if elevated B2M plasma levels led to a higher CLL-IPI risk category.

Results:

Of 299 CLL patients identified, 95 were excluded from further analysis due to missing TP53 mutation assessment. Our cohort included 204 CLL patients with a median age at diagnosis of 64 years (range: 37 – 86) and a female-to-male ratio of 1:2. CKD was evident in 19.1% of patients. CLL-IPI risk groups were balanced among patients with and without CKD (Figures 1, 2). With a median follow-up of 102 months (range: 2 – 360 months) 51.5% of patients eventually met criteria for specific CLL treatment. Median TTFT was similar in non-CKD and CKD patients (Figure 3), but the CLL-IPI did not allow for prognostic discrimination in CKD patients (Figures 4, 5). Although B2M was generally higher in CKD patients (>3.5 mg/L: 31.0% versus 12.7%, p<0.05), elevated B2M remained associated with shorter TTFT (Figure 6). Elevated B2M led to a higher CLL-IPI risk category in 23.1% of CKD patients. Here, B2M>3.5 mg/L was not associated with shorter TTFT anymore (Figure 7) in contrast to patients with low/intermediate risk CLL-IPI (Figures 8, 9).

Conclusion:

Although B2M plasma levels are frequently elevated in CKD patients, B2M>3.5 mg/L remains associated with shorter TTFT. However, the CLL-IPI may not allow for adequate prognostic discrimination, particularly in the subgroup with higher risk CLL-IPI.

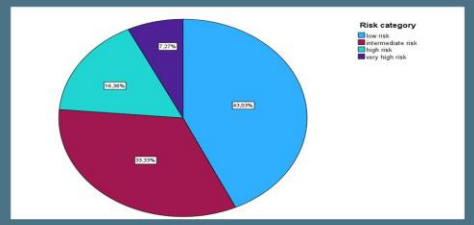

Figure 1: CLL-IPI in non-CKD patients (n=169)

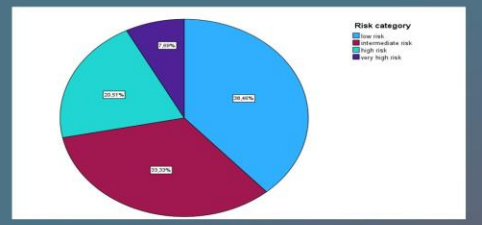

Figure 2: CLL-IPI in CKD patients (n=39)

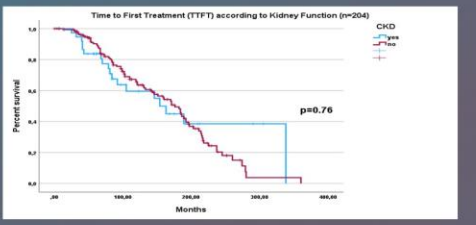

Figure 3: TTFT according to Kidney Function (n=204)

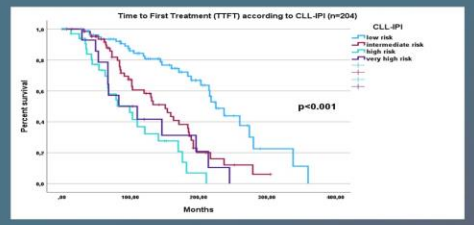

Figure 4: TTFT according to CLL-IPI (n=204)

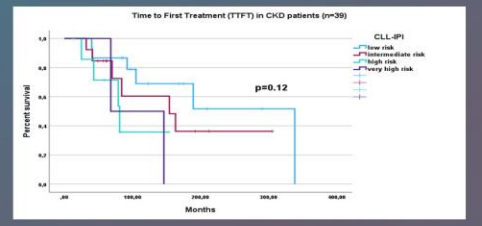

Figure 5: TTFT in CKD patients according to CLL-IPI (n=39)

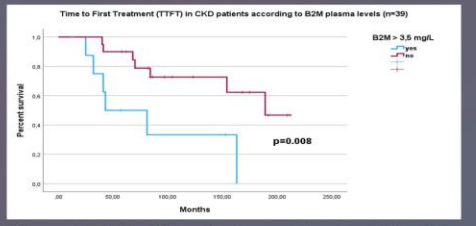

Figure 6: TTFT in CKD patients according to B2M (n=39)

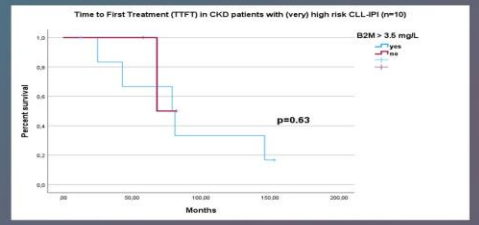

Figure 7: TTFT in CKD patients with high CLL-IPI (n=10)

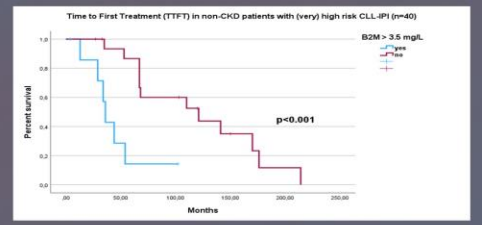

Figure 8: TTFT in non-CKD patients with high CLL-IPI (n=40)

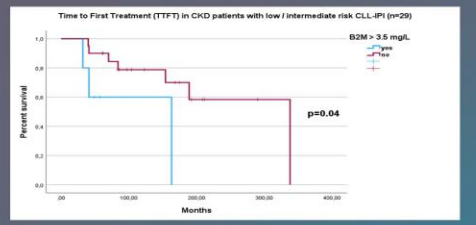

Figure 9: TTFT in CKD patients with low/intermediate CLL-IPI (n=29)

CKD: chronic kidney disease
B2M: Beta-2-Microglobulin

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